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ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.
09/083,793

Applicant(s)
Murphy et al

Examiner
Mary Mosher

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 12/11/00, 5/26/00, 4/9/01

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-94 and 96-143 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1-94 and 96-143 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 11, 19

20) ☐ Other: _____

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DETAILED ACTION

At the outset, the Office wishes to clarify how the claims are being interpreted with regard to the expression vector. On page 7, lines 1-3 of the April 29, 2001 response, regarding claim 55, applicant states, "At the same time, it is noted that the claims are not closed to the possible inclusion of a coinfecting PIV in more detailed embodiments to supplement the claimed method (e.g., by coexpression of one or more of the N, P, or L proteins from the coinfecting virus)." The Office notes that claim 55 depends from claim 52, which states in part, "A method....comprising....coexpressing in a cell or cell-free system an expression vector....and **an expression vector which comprises one or more polynucleotide molecules encoding N, P, and L proteins**" (emphasis added). The Office agrees that the "comprising" term indicates that the claim is open to addition of additional materials, including addition of a coinfecting PIV. However, the coinfecting PIV cannot replace the expression vector (vectors?) which encode N, P, and L proteins on one or more polynucleotide molecules, as the claim is currently drafted. Therefore, claim 52 requires all three of N, P, and L to be expressed from one or more polynucleotides in an expression vector, but does not exclude a coinfecting PIV to express even more N, P, L, or other proteins.

Information Disclosure Statement

The Information Disclosure Statement filed 5/26/2000 (and the copy filed 4/9/2000) have been considered. Any inconvenience the late consideration of this Statement caused applicant is regretted.

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Claim Rejections - 35 USC § 112

Claim 111 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record. This rejection is directed to the confusion in claim 111 regarding the simultaneous requirement for chimerism of the genomes of least two species of PIV and the requirement for "a full complement" of attenuating mutations present in JS cp45, which is one species of PIV with mutations throughout all parts of the genome. Applicant has amended claims 39, 131, and 139 so as to overcome this rejection; however, claim 111 was not amended.

Claims 15, 16, 30, 31, 36, 37, 39, 65- 69, 71, 72, 78, 81, 82, 105, 106, 109-111, 113, 114, 117, 127, 128, 130, 131, 133, 135, 138, 139 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for reasons of record. This rejection is directed to a deposit requirement. Applicant has filed evidence that the necessary deposit has been made under Budapest conditions, and amended the specification to refer to the deposit. However, applicant still has not provided the required assurance that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent. This assurance can be made via an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by

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an attorney of record over his or her signature. In addition, the specification should also include the date of the deposit, see 37 CFR 1.809(d).

Claim Rejections - 35 USC § 102 and § 103

Claims 1-4, 6, 7, 10-17, 20, 21, 26, 27, 30, 33-40, 43, 44, 47-49, 52, 54, 56, 57, 59, 61-85, 88-91, 93, 94, 96-116, 118, 120-143 are rejected under 35 U.S.C. 102(e) as clearly anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Belshe et al (5, 869,036, hereafter abbreviated as "Belshe"), for reasons of record.

Applicant's arguments filed April 9, 2001 have been fully considered but were not found persuasive. Applicant argues that the actual evidence presented by applicants in their extensive prior response (6/19/2000) was largely ignored. The Office notes however that what was presented in the 6/19/2000 response was argument of counsel, including many assertions regarding facts, not actual evidence. These assertions were not ignored, though their probative weight is not the weight of actual evidentiary showings. For the sake of argument though, the Office assumed all of the asserted "facts" could be documented by material in the specification or in printed publications or by declaration. Even based on this assumption, the Office remains unpersuaded and thus, did not require the same information presented in another format. Applicant argues that the Office imposed a burden on applicants to show critical process steps or starting materials to distinguish the claims over the Belshe disclosure. To the extent that applicant is challenging the validity of an issued U.S. patent, the law imposes a burden upon applicant to establish that the patent's disclosure is not sufficient to support the patent claims.

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This imposition is based upon the presumed validity of a U.S. patent. Clear and convincing evidence of nonenablement is generally required.

In the 6/19/00 response, regarding the alleged deficiencies of Belshe, applicant argued that no cDNA constructs were designed and produced from which PIV3 wild type viruses could be recovered, and certainly no constructs of recombinant viruses bearing specific attenuating mutations were produced. Applicant argues that resolving these deficiencies was critical to enablement of applicant's claimed invention, and the absence of such disclosure in the Belshe reference defeats any reasonable expectation for success to achieve applicant's invention. However, see patent column 9, line 55 to column 10, line 40, which discusses producing a cDNA and recovering a virus. Applicant's arguments amount to an assertion that working examples are required for enablement of the patent claims. However, working examples are not required for enablement, though they are one factor to consider.

Applicant argues that the deficiencies of Belshe are especially clear when the particular results achieved by applicants are considered, namely that it was shown to be possible to construct recombinant PIV vaccine candidates from cDNA that are suitably attenuated, yet sufficiently immunogenic to produce a protective immune response in immunized hosts. Applicant discussed complexities of temperature sensitivity and attenuation, differences between in vitro and in vivo results, particularly differences in actual host animal temperature, and different levels of temperature sensitivity from different mutations and combinations of mutations. While applicant clearly has characterized attenuating mutations in detail, and has a specification that goes well

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beyond the disclosure of Belshe, the rejected claims are not limited to those aspects of the invention which go beyond the subject matter of the claims of Belshe. Belshe's alleged failure to identify specific properties determined by individual cp45 L gene mutations or to reliably predict combinatorial phenotypes specified by sets of mutations incorporated within novel vaccine candidates analyzed in vivo, simply is not commensurate in scope with the rejected claims. The rejected claims are not limited to individual cp45 mutations not taught by Belshe, or to combinations with unexpected phenotypes.

Applicant further argues that it was unknown if successful recovery would require expression of the D ORF. However, applicant's claims do not require expression of the D ORF, thus leading to the conclusion that the D ORF is not required for success. Applicant argues that the complementation method used by Belshe is not adequate to forecast that a recombinant virus bearing one or more of the cp45 mutations would be attenuated in vivo, and argues that one combination discussed by Belshe was overattenuated and another combination was less attenuated than cp45. However, it appears that both combinations, as recited in the patent claims, were actually attenuated and temperature sensitive even if they may not have reached an ideal degree of temperature sensitivity and attenuation. Therefore this does not serve as evidence of nonenablement of the patent claims. Applicant discusses, at length, differences between applicant's disclosure and Belshe's disclosure, pointing to many mutations outside the L region which were found to be attenuating. This extensive discussion involves limitations which are not in the rejected claims and is also not commensurate in scope with the rejected claims.

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The prior response was not ignored. On the contrary, the prior response has been carefully and fully considered to determine whether a clear and convincing evidentiary case of nonenablement was made regarding the disclosure and patented claims of Belshe, when the disclosure was combined with the skill of those in the art and routine experimentation. Absent such evidence, and absent some claim limitation which distinguishes applicant's claims from the patent claims, a patent examiner has no authority to allow claims that are anticipated (or very nearly anticipated) by prior patent claims. The Office is aware that applicant presents working examples in the specification, while Belshe et al does not. The Office understands that applicants analyzed the phenotypes of the resulting viruses in detail, discovering that some combinations of point mutations did not produce the phenotype one would have expected from the teachings of the Belshe patent. However, the record in this application does not provide clear and convincing evidence that one skilled in the art would have been unable to produce the materials recited in the patent claims, using the disclosure in the patent and routine experimentation. Therefore the arguments are not convincing, and the rejection is maintained.

Claims 51 and 53 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe et al, for reasons of record.

Claims 18, 19, 28, and 29 remain rejected under 35 U.S.C. 102(e) as anticipated by Belshe et al, or, in the alternative, under 35 U.S.C. 103(a) as obvious over Belshe et al in view of Stokes et al (Virus Research 30:43-52, 1993), for reasons of record.

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Claims 22-25, 31, 32, 42, 60, 117, and 119 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Belshe et al in view of Conzelmann (Journal of General Virology 77:381-389, 1996) for reasons of record.

Claims 91 and 92 remain rejected under 35 U.S.C. 102(b) as being anticipated by Dimock et al (Journal of Virology 67:2772-2778, 1993) for reasons of record.

Applicant argues that the defective particles of Dimock do not represent "an infectious PIV particle" However, Dimock et al states in the Abstract that the defective genomes "were packaged into particles that could be used to infect fresh cells." Therefore the defective particles of Dimock were indeed infectious. Claims 91 and 92 do not require the particles to be self-replicating. The specification, on page 6, defines a subviral particle as any infectious PIV particle which lacks a structural element; the defective particles of Dimock et al meet this definition. Although the defective particles of Dimock are indeed different from the viruses made by applicant, they fit squarely within the bounds of these claims.

The rejection of claims 11, 48, 50, 52, 55, 56, 58, under 35 U.S.C. 102(b) as being anticipated by Dimock et al (Journal of Virology 67:2772-2778, 1993), is withdrawn in view of applicant's arguments and amendments to the claims. On reconsideration, the deleted PIV genome of Dimock et al is not capable of yielding an infectious PIV particle upon coexpression with PIV N, P, and L proteins, because the deleted genome lacks genes encoding other proteins required to complete the infectious particle. If native PIV is not encompassed within the phrase

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“expression vector”, then Dimock et al does not coexpress the deleted PIV genome with an expression vector encoding N, P, and L proteins. .

Double Patenting

Claims 1-94 and 96-143 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6, 8-45, 47-50 of copending Application No. 09/458,813, for reasons of record.

Claims 1-94 and 96-143 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-58 of copending Application No. 09/459,062, for reasons of record.

Applicant’s intent to address these rejections later is noted. The rejections are repeated to indicate that they are not withdrawn.

NEW GROUNDS OF REJECTION

Double Patenting

Claims 1-94 and 96-143 of this application conflict with claims 1-94 and 96-128 of Application No. 09/424,628, as the ‘628 claims are identical to the originally-filed claims of this application. 37 CFR 1.78(b) provides that when two or more applications filed by the same applicant contain conflicting claims, elimination of such claims from all but one application may be required in the absence of good and sufficient reason for their retention during pendency in more than one application. Applicant is required to either cancel the conflicting claims from all but one application or maintain a clear line of demarcation between the applications. See MPEP § 822.

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Claims 1, 2, 5-10, 33-42, 73, 74, 76-80, 83, 88, 89, 97-99, 107-111, 122, 123, and 141 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-83 of copending Application No. 09/586,479. Although the conflicting claims are not identical, they are not patentably distinct from each other because the copending claims to HPIV/BPIV chimeras are within the scope of the instant claimed PIV chimeras.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Applicant is warned that still more double patenting issues may arise once the examiner has access to any recently filed applications.

Claim Rejections - 35 USC § 112

Claims 1-94 and 96-143 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the viruses disclosed in the working examples, does not reasonably provide enablement for the full scope of viruses encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims. Applicant now takes the position that “useful mutations for incorporation in Applicant’s recombinant vaccines can only be defined by actual recovery of the mutations in a recombinant virus, and by demonstration that the mutations specify desired phenotypes in the recombinant virus.” See response page 22. Since this is applicant’s position, it is perfectly reasonable to require applicants

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to satisfy their own precondition for enablement. Applicant's response also includes arguments directed to the unpredictable additive effects of multiple mutations. Accepting applicant's own characterization of the art, and applicant's own arguments on the unpredictability of untested combinations, it is impossible to avoid the conclusion that the specification is enabling only for the mutations defined by actual recovery in a recombinant virus and demonstrated to specify desired phenotypes. Furthermore, considering the unpredictable effects of combination of multiple mutations, as set forth in applicant's arguments, it is impossible to avoid the conclusion that the specification is enabling only for the mutation combinations set forth in the working examples. The previous rejection of claims directed to chimeric viruses is seen as moot in light of the even higher standard for enablement presented by the arguments in applicant's latest response.

Response to Arguments

Applicants are not correct in asserting that they are being held to a standard higher than *Belshe*. The same statutory requirements apply to all applications equally. However, when one is asserting that one or more U.S. patent claims are not enabled, the burden is heavy since there is a presumption that those claims are fully enabled at the time of issuance. Further, each application is considered on its own merits, and the merits for this application include applicant's own characterization of the state of the art and the predictability of the art, which are factors to be considered in regard to enablement of the claims in this application. Each communication from applicants includes statements which require re-evaluation of the predictability of the art which

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may or may not necessitate additional rejections or extending rejections to additional ones of applicant's claims.

The merits for this application also include the presence of subject matter, within the scope of the application claims, which is recited in the claims of an issued patent. Applicant's opinion of the state of the art and the unpredictability of the art does not constitute clear and convincing evidence that one skilled in the art would not have been able to produce the materials of the patent claims using the disclosure of the patent specification and routine experimentation. Absent clear and convincing evidence to the contrary, the patent claims are presumed enabled, and in the face of this presumption applicant's claims remain rejected as anticipated by the patent claims, or as obvious over the patent claims as stated above.

Conclusion

This action is nonfinal, as the new grounds of rejection were necessitated, not by amendment to the claims, but by applicant's arguments and by newly available copending applications.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mary E. Mosher, Ph.D. whose telephone number is (703) 308-2926. The examiner can normally be reached on Monday -Thursday and alternate Fridays from 6:30 AM to 4:00 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is now (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

June 18, 2001

Mary Mosher
MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800
1600